

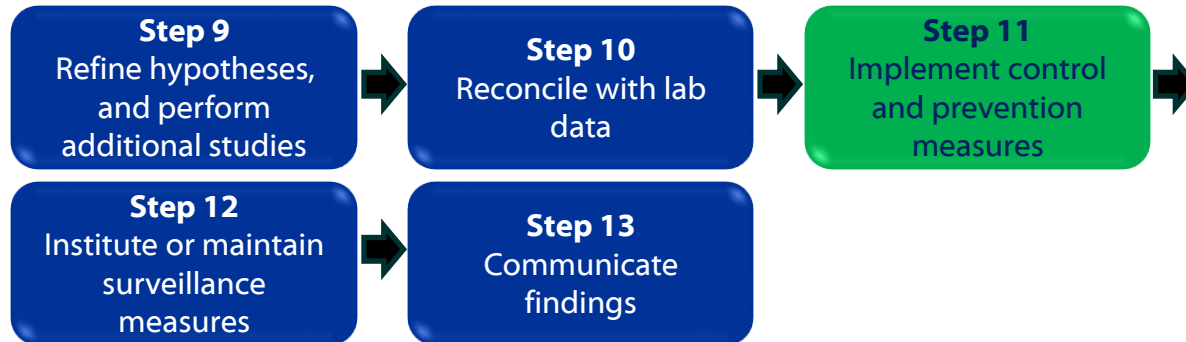
# Toxicological Outbreak Investigation

## Module 5: Steps of a Toxicological Outbreak Investigation, Part 3



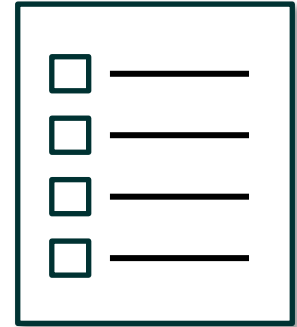
# Welcome

- Welcome to Module 5 Part 3 of Toxicological Outbreak Investigation. This training follows the general steps outlined in CDC's Principles of Epidemiology in Public Health Practice: An Introduction to Applied Epidemiology and Biostatistics, 3<sup>rd</sup> edition.
- In this module, we will discuss steps 9–13 in an outbreak investigation.
- This module should take about 40 minutes to complete.



# Objectives

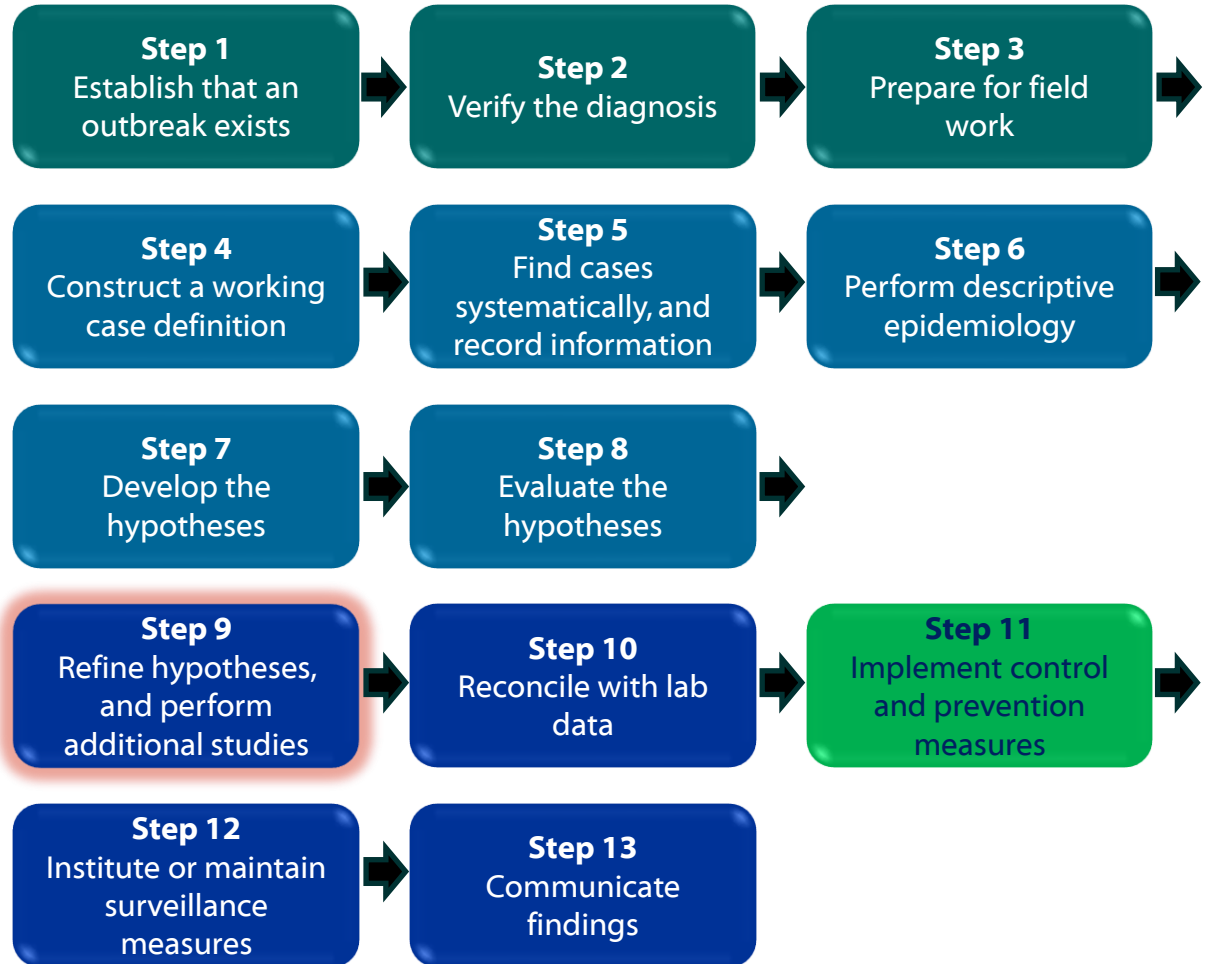
- After completing this course, you will be able to
  - Refine hypotheses and perform additional studies
  - Reconcile epidemiologic data with lab data
  - Implement control and prevention measures
  - Initiate or maintain surveillance measures
  - Communicate findings



# Steps in an Outbreak Investigation

Depending on the circumstances, some of these steps might be done in a different order.

Implementing control and prevention measures should be a constant consideration. This should be done as soon as there is information to support such actions.



# Refining Hypotheses

- Based on initial studies, additional studies might be planned to further refine the hypotheses.
- This might include additional epidemiologic studies or laboratory analyses.



## Scenario: Next Steps

- Let's return to our scenario from earlier in Module 5.
- Based on the findings of the epidemiologic study, the team advised the laboratory to analyze urine samples collected from students at the school and samples of the snacks.



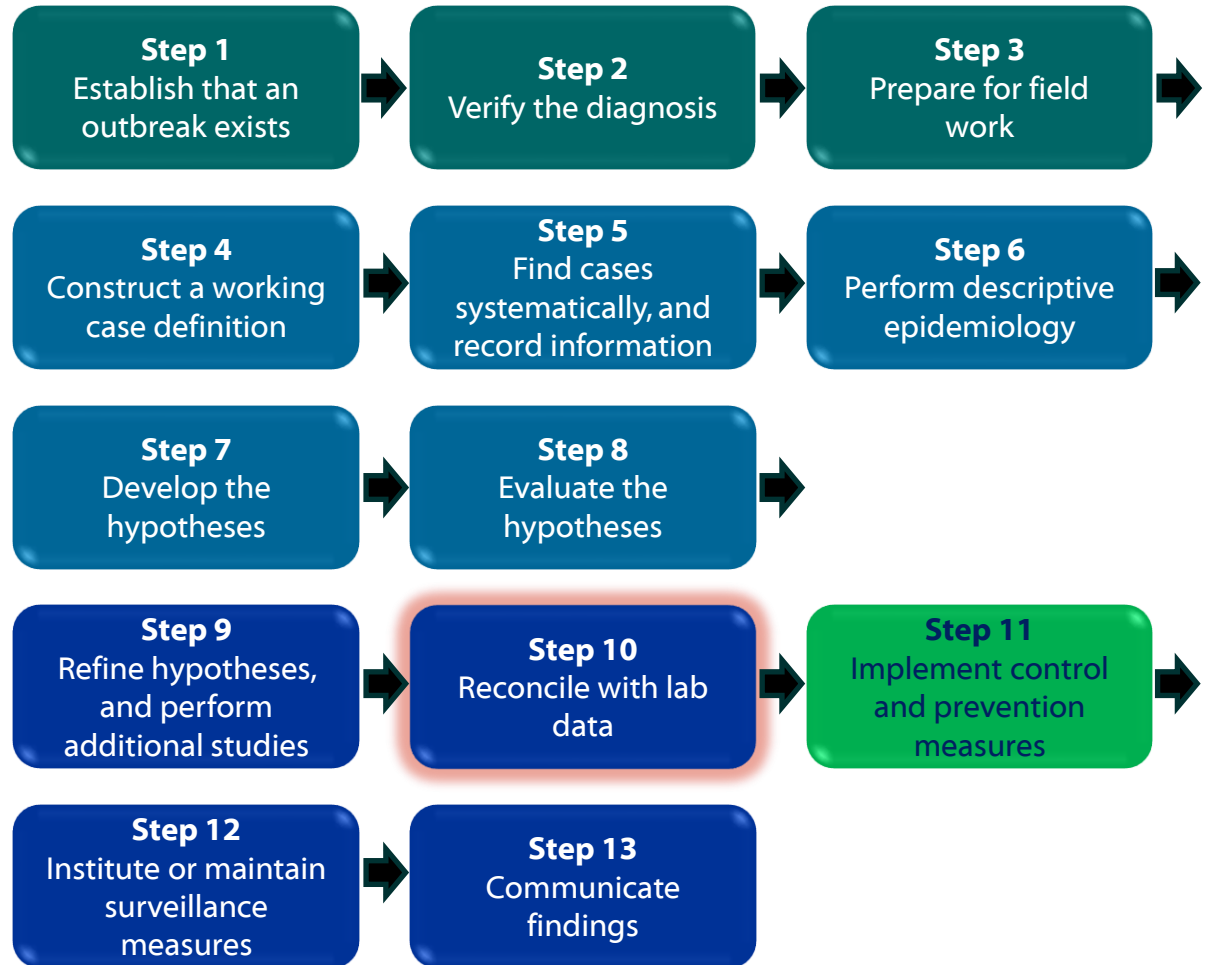
# Scenario: Next Steps

- Tested toxic agents were selected based on the following considerations:
  - Toxic agents that could cause the symptoms that were observed among ill people
  - Toxic agents thought to be potentially present (e.g., observed in the places where people became ill or where food was prepared)
- In the scenario, toxic agents that met these criteria included
  - Toxic metals (mercury, etc.)
  - Herbicides (paraquat, etc.)
  - Metabolic poisons (cyanide, etc.)

# Steps in an Outbreak Investigation

Depending on the circumstances, some of these steps might be done in a different order.

Implementing control and prevention measures should be a constant consideration. This should be done as soon as there is information to support such actions.



# Evaluating Laboratory Results

- Several considerations need to be kept in mind when analyzing and interpreting laboratory data:
  - Limit of detection
  - Making adjustments
  - Examining the distribution of measured concentrations in biological samples among study participants
  - Using appropriate comparison values
  - Considering the circumstances of sample collection (e.g., timing, sampling strategy)
- Module 3 (Toxicological Laboratory Principles) and Module 4 (Analyzing and Interpreting Laboratory Results) include more details on these topics.

# Scenario: Laboratory Testing Results

- Continuing with the scenario presented earlier, the investigators receive laboratory data from testing done on the urine specimens collected from students at the school, including students who were ill and those who were not ill.
- The results include urine concentrations of cyanide, mercury, and paraquat.

## Scenario: Laboratory Testing Results (cont.)

- *Based on the results shown below for urine cyanide concentrations, could cyanide have been the culprit?*

Cyanide (ng/mg creatinine)	Specimens from people who were ill	Specimens from people who were not ill
% above the limit of detection	0%	0%
Range	N/A	N/A
Median	<LOD	<LOD



## Scenario: Laboratory Testing Results (cont.)

Cyanide (ng/mg creatinine)	Specimens from people who were ill	Specimens from people who were not ill
% above the limit of detection	0%	0%
Range	N/A	N/A
Median	<LOD	<LOD

- Although it seems unlikely that cyanide is the culprit because no cases had detectable levels, it is theoretically possible that it could have been.
- Possible reasons why cyanide was not detected include
  - The specimens could have been collected after cyanide was already eliminated or metabolized.
  - The levels at which symptoms may be observed might be lower than the limit of detection.

## Scenario: Laboratory Testing Results (cont.)

- Results for urine mercury concentrations are shown below.
- These results show that mercury was frequently detected in specimens from people who were ill and from people who were not ill, and concentrations are slightly higher than the general population from NHANES data.
- Does this mean that mercury is causing the illness?

<b>Mercury (<math>\mu\text{g/L}</math>)</b>	<b>Specimens from people who were ill</b>	<b>Specimens from people who were not ill</b>
% above the limit of detection	80%	60%
Range	<LOD–3.66	<LOD–2.97
Median	2.02	1.96

## Scenario: Laboratory Testing Results (cont.)

Mercury ( $\mu\text{g/L}$ )	Specimens from people who were ill	Specimens from people who were not ill
% above the limit of detection	80%	60%
Range	<LOD–3.66	<LOD–2.97
Median	2.02	1.96

- The fact that mercury is present in slightly higher concentrations in urine from both people who were and were not ill does not mean that it is causing the illness.
- The fact that the median level is similar between people who were and were not ill suggests that it did not cause the outbreak, although there could be another factor influencing susceptibility to illness resulting from mercury exposure that could differ between those who were and were not ill.

## Scenario: Laboratory Testing Results (cont.)

- Paraquat was detected in a higher proportion of specimens and had a higher median concentration among specimens from people who were ill compared with specimens from people who were not ill.
- Does this mean it caused the illness?

<b>Paraquat (<math>\mu\text{g}/\text{ml}</math>)</b>	<b>Specimens from people who were ill</b>	<b>Specimens from people who were not ill</b>
% above the limit of detection	90%	10%
Range	<LOD–41	<LOD–0.1
Median	23.5	<LOD

## Scenario: Laboratory Testing Results (cont.)

Paraquat ( $\mu\text{g}/\text{ml}$ )	Specimens from people who were ill	Specimens from people who were not ill
% above the limit of detection	90%	10%
Range	<LOD–41	<LOD–0.1
Median	23.5	<LOD

- Based on these data, it would be reasonable to conclude that paraquat likely caused the outbreak.
- It is not a substance that would typically be expected to be found in biologic specimens, so its presence would indicate that it likely caused the illness.

# Interpretation of Laboratory Values: Comparison Values

- Interpreting laboratory values generally requires some source of comparison values.
- Comparison values could come from various sources:
  - Comparison samples collected as part of the outbreak investigation, such as from controls in a case-control study or from people who did not become ill in a cohort study
  - Established levels associated with symptoms or illness
  - Other sources of comparison values

# Interpretation of Laboratory Values: Levels Associated with Illness

- For some toxic agents, the levels or concentrations that are associated with illness are known.
  - IF concentrations in specimens from people who are ill are **higher** than these levels, AND their clinical presentation is consistent with exposure to the toxic agent, THEN you might conclude that the toxic agent caused the outbreak.
  - IF concentrations in specimens from people who are ill are **lower** than these levels, BUT the clinical presentation of people who are ill resembles what would be expected following exposure to that toxic agent, THEN it might mean that
    - the toxic agent did not cause the outbreak, or
    - the specimens were not collected soon enough following exposure, and perhaps the toxic agent was already partly eliminated from the body.
    - additional factors were not optimal, such as the laboratory method used, specimen collection and storage, etc.

# Interpretation of Laboratory Values: Other Sources of Comparison Values

- The National Health and Nutrition Examination Survey (NHANES) provides a wealth of information for biomonitoring levels:

<https://www.cdc.gov/exposurereport/>

- If comparison values are not available from an appropriate study as part of the outbreak investigation and established levels associated with illness are not available, sources such as NHANES can help put the observed concentrations in biological samples into context.
- However, there might be reasons unrelated to the outbreak why specimens collected from particular populations have overall levels of a toxic agent that might be considered high based on levels observed in NHANES.

## Scenario: Environmental Laboratory Data

- Investigators also received the data below from laboratory measurements done on the snack samples.
- Why do you think paraquat was not detected in one of the snack samples?

Toxic Agent	Piece #1	Piece #2	Piece #3	Piece #4	Piece #5
Cyanide ( $\mu\text{g/g}$ )	<LOD	<LOD	<LOD	13	<LOD
Mercury ( $\text{ng/g}$ )	<LOD	<LOD	<LOD	<LOD	5
Paraquat ( $\text{ng/g}$ )	331	20	<LOD	648	394

## Scenario: Environmental Laboratory Data (cont.)

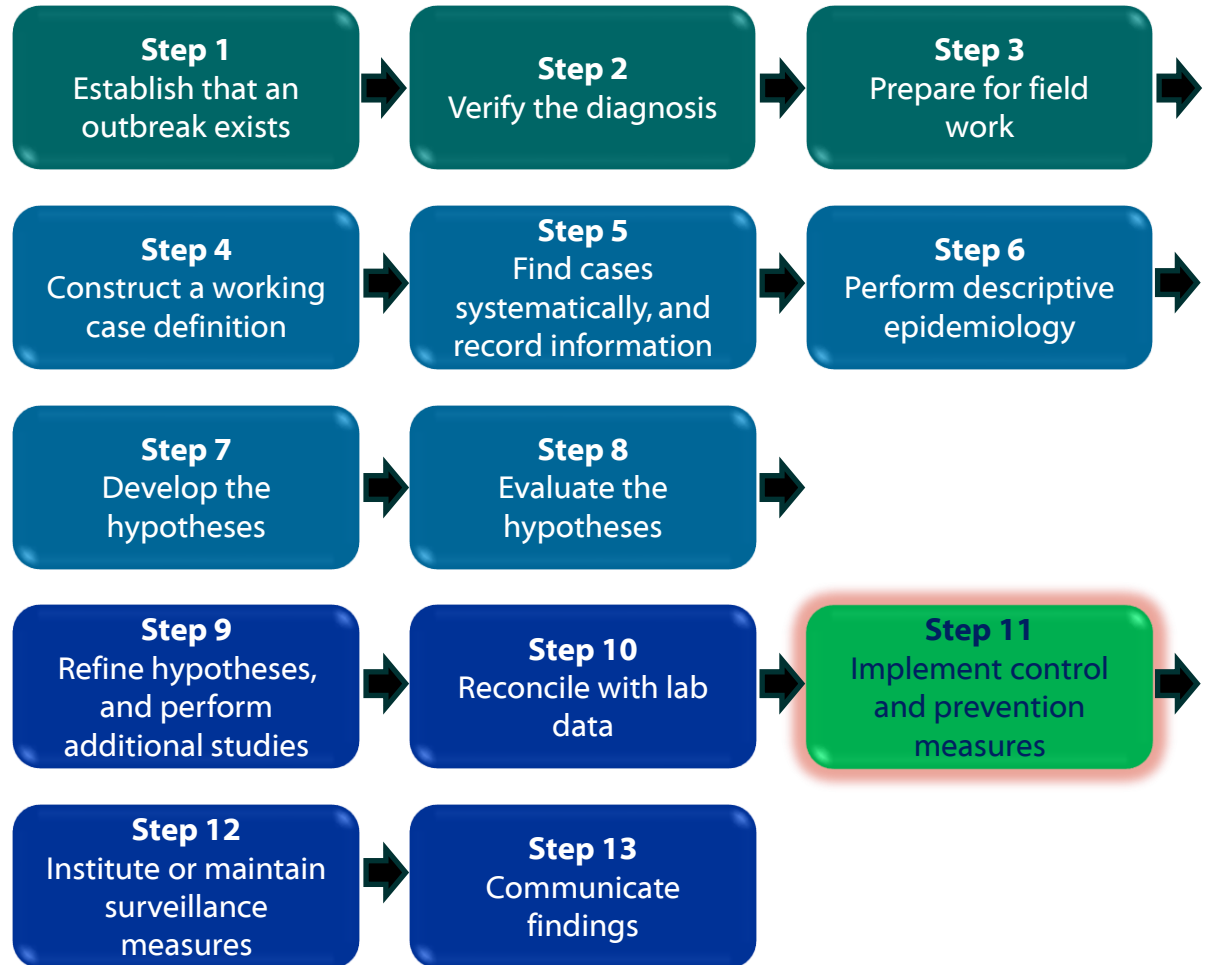
Toxic Agent	Piece #1	Piece #2	Piece #3	Piece #4	Piece #5
Cyanide ( $\mu\text{g/g}$ )	<LOD	<LOD	<LOD	13	<LOD
Mercury ( $\text{ng/g}$ )	<LOD	<LOD	<LOD	<LOD	5
Paraquat ( $\text{ng/g}$ )	331	20	<LOD	648	394

- The paraquat was probably not detected in piece #3 because of heterogeneous distribution in the snack.
- This is a good example of why it is important to take more than one sample of environmental media.

# Steps in an Outbreak Investigation

Depending on the circumstances, some of these steps might be done in a different order.

Implementing control and prevention measures should be a constant consideration. This should be done as soon as there is information to support such actions.



# Control Measures

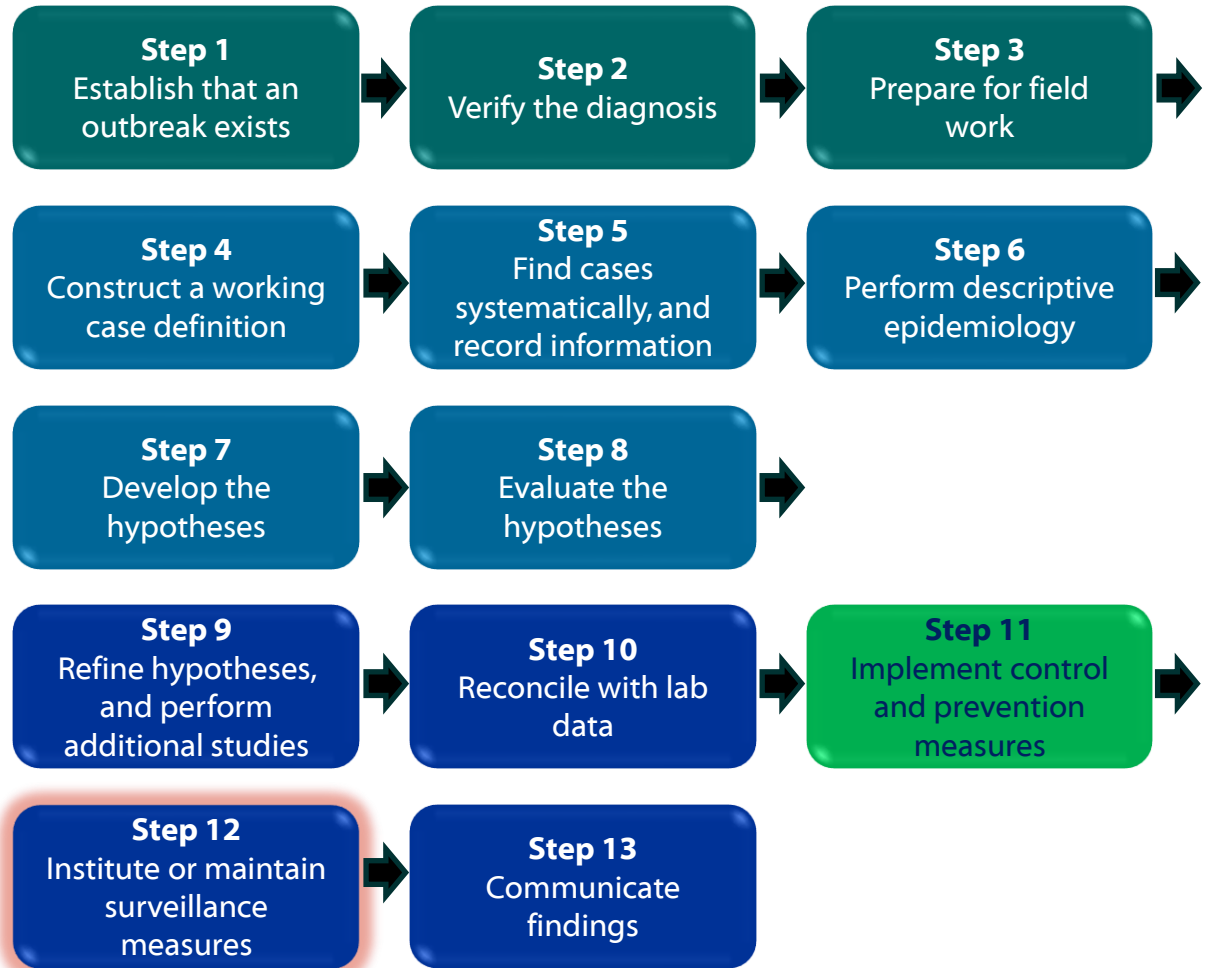
- Every outbreak investigation is unique; therefore, control measures are also unique.
- Control measures should be implemented as soon as there is evidence to support them and might be implemented in stages.
- Examples
  - Following an investigation like the one in the scenario, if the snack was prepared at a home, local investigators might first make sure any leftover snack is not eaten and then investigate the snack ingredients to determine how herbicide contamination could have occurred. They might take other actions based on the findings.
  - For an outbreak involving a commercial food product, a regulatory agency (e.g., FDA in the U.S.) might get involved to determine how the contamination occurred, and the product might be recalled.
  - Other types of outbreaks might involve various interventions, such as public education, medical prevention measures, or others, as appropriate.



# Steps in an Outbreak Investigation

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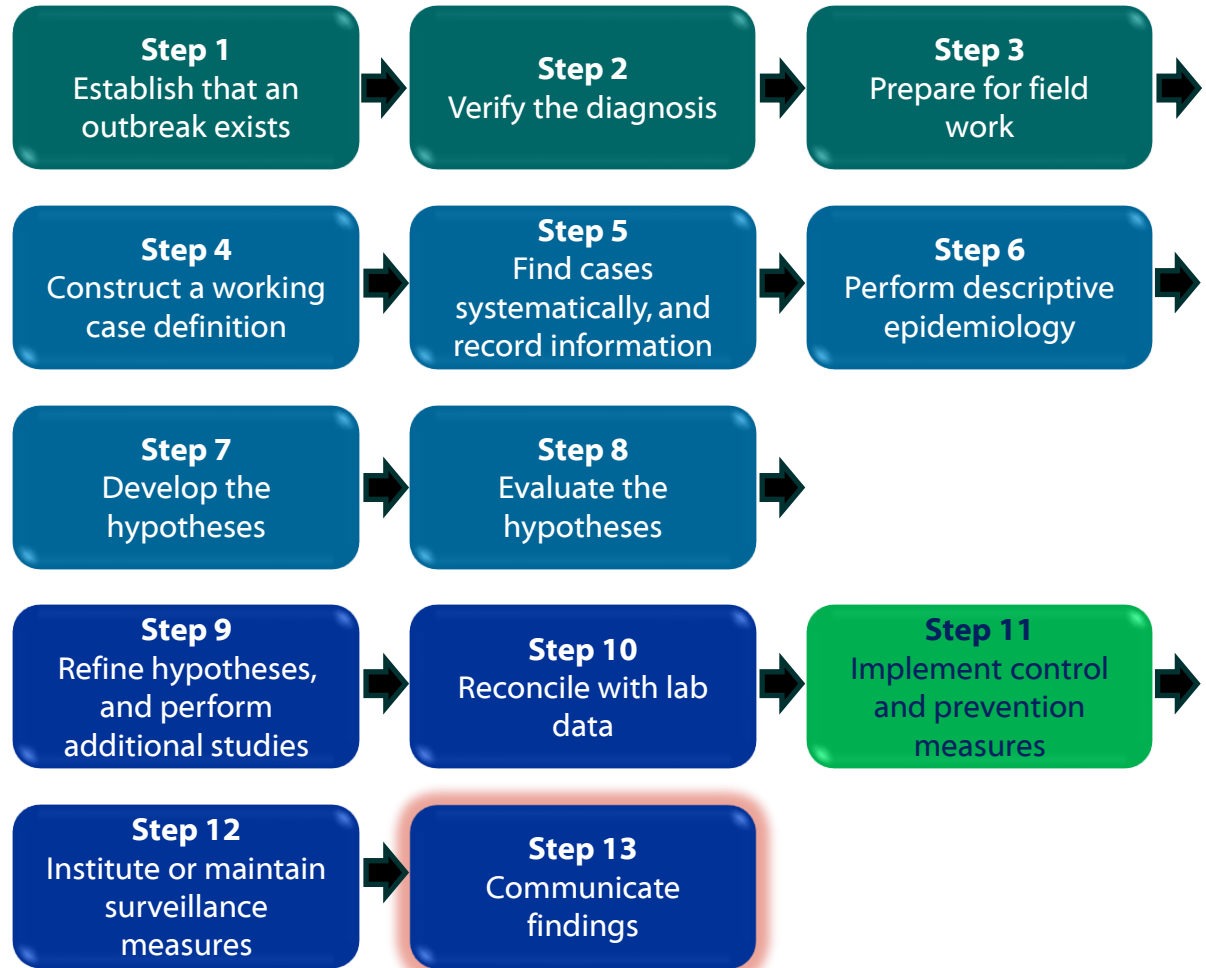
# Identifying Additional Cases and Notifying the Community

- Depending on the situation and resources, you may or may not decide to implement a surveillance system.
- Example: Following an investigation like the one in the scenario, a campaign might be started to inform the public, school officials, and healthcare providers that they should report food poisoning to public health officials.

# Steps in an Outbreak Investigation

Depending on the circumstances, some of these steps might be done in a different order.

Implementing control and prevention measures should be a constant consideration. This should be done as soon as there is information to support such actions.



# Communicating Findings

- Throughout the investigation, investigators should have a plan for communicating with important stakeholders and the public.
  - This will vary from outbreak to outbreak.
  - It can be helpful to designate a spokesperson to be the primary communicator.
- At the conclusion of an investigation, it is important to summarize the findings and recommendations for stakeholders. This can include the following:
  - Presentations
  - Reports
  - Publications

## Communicating Findings (cont.)

- For toxicological outbreaks, toxicological laboratory results can sometimes be difficult to explain to stakeholders.
- Two key communication issues that can arise include the following:
  - Explaining why a specific toxic agent was not found, particularly if it is believed to have caused the outbreak
  - Explaining why finding specific toxic agents in samples does not necessarily mean they caused the outbreak

# False Negative Results

- It is not always possible to identify the etiologic agent in an environmental or biologic sample.
- Reasons for a false negative result can include
  - A level associated with illness that is lower than the limit of detection
  - A toxic agent that has a short half-life, and was metabolized, eliminated, or degraded before the sample was collected
  - Inadequate sample quality or quantity

## Scenario: Explaining Positive Results

- *What are some possible talking points for explaining why mercury was detected in some biologic specimens in the previous scenario?*

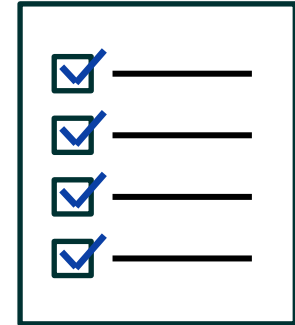


## Scenario: Explaining Positive Results (cont.)

- Some possible talking points might include the following:
  - Mercury was detected in urine specimens from a majority of students from whom specimens were collected, including students who were not ill.
  - Although mercury is a neurotoxin, it is unlikely that mercury contributed to the outbreak.
  - The levels of mercury are within the range of levels typically found in the U.S. population.
  - There are many possible sources of mercury exposure, including fish.

# Module Summary

- This concludes Module 5 Part 3.
- In this module, we discussed steps 9–13 of a toxicological outbreak investigation, which include
  - Refine hypotheses and perform additional studies
  - Reconcile with lab data
  - Implement control and prevention measures
  - Initiate or maintain surveillance measures
  - Communicate findings
- You should now be able to
  - Apply outbreak investigation steps 9–13 to a toxic agent outbreak
  - Describe the purpose of the materials in the Toxicological Outbreak Tool Kit



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